REMARKS/ARGUMENT

Claims 1-22 are active.

Claim 1 is amended to exclude compounds from the proviso that are no longer present based on the previous amendment to the G substituent as noted in the Action. Accordingly, the rejection under 35 USC 112, second paragraph can be withdrawn.

Applicants thank the Examiner for the courtesy of discussing this case with their undersigned representative by telephone on June 21, 2011. The substance of this discussion is reflected and expanded upon in the remarks below.

The Examiner newly rejects Claims 1, 2, 4, 5, 11, and 21 as obvious in view of Yoneda and Unangst (see page 5 of the Action). Applicants respectfully disagree.

The inventors have discovered that the presently claimed compounds are particularly effective as PI3 kinase inhibitors. See, e.g., the paragraph bridging pages 6-7 in the present specification. The cited references do not disclose or suggest the claimed compounds.

In the Office Action, the Examiner cites to a compound (see page 5) in Yoneda, which appears to be Example 4 in col. 4 and states that this compound is similar to what is defined in the present claims with the difference between a cyano group in the Yoneda compound and a C1 alkoxy at the G position. Thus, the Examiner argues that because Yoneda discusses the publication of Unangst and one of the compounds, 8f, includes a methoxy at the corresponding G position, one would have found it obvious to first choose Example 4 and then modify it to replace the cyano group with the methoxy group from a structurally unrelated compound, i.e., note the absence of the dioxolane in the Unangst general formula at the top of page 324 cited by the Examiner. Indeed, the compounds identified in Table 3 are significantly different structurally to that which is claimed and provide little guidance as to altering a substitutent on a very different compound, even like that one in Yoneda.

This line of argument is flawed because when considered as a whole, the combined teachings of Yoneda and Unangst would not have suggested the presently claimed compounds because there are numerous points of substitution that could have taken place and if one took into account the full scope of the art, any one of the positions could have been changed leading to potentially thousands of possible compounds. This is not a sufficient basis to argue that the claims would have been obvious. Even with the combined teachings of Yoneda and Unangst there is no teaching which would have lead one of skill in the art to select the one particular substitution of the one specified Example cited in the Office Action.

Even post KSR, for a claimed invention to be obvious, the possible modifications of the prior art must be finite. *See, Rolls-Royce PLC v. United Technologies Corp.*, 95 USPQ2d 1097 (Fed. Cir. 2010). As stated by the Federal Circuit:

To determine that an invention would have been obvious to try on the basis of the record before the time of invention, this court has clarified, with respect to inventions requiring selection of a species from a disclosed genus, that the possible approaches and selection to solve the problem must be "known and finite." See Abbott, 544 F.3d at 1351 (holding as conditions in which "obvious to try" may negate patentability, "the problem is known, the possible approaches to solving the problem are known and finite, and the solution is predictable through use of a known option"). . . . In this case, the broad selection of choices for further investigation available to a person of ordinary skill included any degree of sweep. See Takeda, 492 F.3d at 1359 (holding the invention not obvious to try because the prior art disclosed a broad selection of compounds that an ordinarily skilled artisan could have selected for further investigation).

Rolls-Royce, at 1107, emphasis added.

This case is like that in Rolls-Royce in that there are countless possible theoretical modifications of the prior art with no teaching that any one modification should be selected. Yoneda discloses a general formula in col. 1, each with any number of differences. However, absent hindsight disclosure as to which substituent to change, any of the positions, indeed any of the rings or core could be changed. For example, looking at the formula in col. 1, there are several positions that can be changed based on the Examiner's unsupported contention that it

would have been obvious to change the Yoneda compounds. So but for hindsight to specifically select one position out of the many possible or so that are disclosed in Yoneda (whether variable or not, i.e., not limited to the Rgroups) the possible combination of substituents stems yields hundreds of thousands of possible combinations and perhaps even higher.

Thus, when one considers the citations as a whole it can be seen that the number of theoretical substitutions for compounds such as that of Claim 1 are exceedingly high. There are no teachings that would have led one of ordinary skill in the art to select one particular substitution cited in the Office Action. According to US law the possible modifications of the prior art must be finite and as clear from the general formulas provided in Yoneda there are countless possible theoretical modifications of the prior art with no teaching that any one modification should be selected over another to arrive at the claimed compound.

Further and even if one focused on Example 4 as the Examiner has done, why would one specifically change the cyano group to a methoxy group when any of the position and even rings could be changed. Indeed, following the Examiner's rationale of combining Unangst with Yoneda, one of skill may also consider removing the dioxolane group and its place provide the hydroxyl and two tert-butyl substitutents. This construction of the prior clearly screams of hindsight reconstruction of the present claims.

While Applicants acknowledge the Examiner's rationale set forth on pages 7-8 of the Action, citing the case of *Eisai Co. Ltd v Dr. Reddy's Laboratories*, the key phrase in the quoted portion is the "lead compound" How is it that Example 4 is chosen from all of the compounds in the Examples and particularly within the scope of the general formula taught in col. 1? Indeed, this was clearly done in hindsight, which is improper, when considering the teachings of Yoneda as a whole. Most notably, one of skill in the art following Yoneda's teachings would NOT have selected Example 4 as the lead compound because its activity was

Reply to the Official Action of March 8, 2011

significantly lower than other compounds, compare the inhibition rate of Examples 2, 8, 10,

13 and 15 to that of Example 4. Identifying a compound as a "lead compound" is central to

this analysis (see, e.g., Procter & Gamble Co. v. Teva Pharms., USA, Inc. 566 F.3d 989, 90

U.S.P.Q.2D 1947 (Fed. Cir. 2009)). Indeed, the Examiner has made no reasonable attempt to

establish a reasonable expectation of success of making the claimed compound having PI3

kinase inhibition activity. (Id.). Notably, in the same Eisai case cited in Procter "To the

extent an art is unpredictable, as the chemical arts often are, KSR's focus on these "identified,

predictable solutions" may present a difficult hurdle because potential solutions are less likely

to be genuinely predictable." Eisai Co. Ltd. v. Dr. Reddy's Labs., Ltd, 533 F.3d 1353, 87

U.S.P.Q.2D 1452 (Fed. Cir. 2008).

It is respectfully requested that the rejection be withdrawn, consider and search the

non-elected species, rejoin the non-elected subject matter and that the Office issue a Notice of

Allowance indicating all pending claims are allowable.

Respectfully submitted,

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17